

matrix, thereby providing a relatively higher spatial resolution for trapping and transporting samples. Second, the microcoil array has a finer degree of magnetic field control than does the microelectromagnet wire matrix and can thus handle a larger number of samples simultaneously; specifically, a  $N \times N$  microcoil array can effectively provide  $N^2$  independent simultaneous local magnetic fields (based on  $N^2$  independent currents), whereas an  $N \times N$  wire matrix can provide only  $2N$  independent simultaneous fields (based on  $2N$  independent currents). Third, as discussed in greater detail below, a microcoil provides a better platform for RF detection owing to its well-defined inductance. Fourth, parasitic magnetic fields due to electrical leads generally are less significant in the microcoil array than in the microelectromagnet wire matrix.

**[0103]** One issue in the design of a two-dimensional microcoil array **200B** according to one embodiment of the present disclosure relates to the magnetic force that can be generated in a plane immediately above and parallel to the array. This plane is indicated generally in both **FIGS. 2 and 6(a)** by an  $x$  axis and  $y$  axis. In particular, the  $x$ - $y$  component of magnetic force generated by the respective microcoils of an array must be large enough to move magnetic samples (e.g., biological cells attached to magnetic beads) that are suspended in a fluid within a reasonable range (e.g., a distance between centers of two neighboring microcoils, or “pitch” of the array, as indicated in **FIG. 6(a)** by the reference numeral **216**) and within a reasonable time (e.g., 1 sec or less), overcoming surface frictions and fluid viscosity. Another design issue relates to magnetic potential energy; to maintain a sufficiently strong trap of a magnetic sample while at the same time suppressing thermal jitters (i.e., Brownian motion) and diffusion due to a thermal energy of the sample, the magnetic potential energy generated by the respective microcoils must be substantially larger than the thermal energy of the sample (i.e.,  $3/2 kT$ , where  $k$  is the Boltzmann constant and  $T$  is the sample temperature). Yet another design issue relates to magnetic force in a direction perpendicular to the plane of the array, along a  $z$  axis as indicated in both **FIGS. 2 and 6(a)** (the  $z$  axis illustrated in **FIG. 6(a)** is in perspective view, and actually points in a direction out of the plane of the figure). Based on the technology and methodology used to fabricate the microcoil array, there may be one or more material layers above the array (e.g., insulating, protecting and or biocompatible material layers, etc.) that extend an appreciable distance above the array along a direction parallel to the  $z$  axis, over which the generated magnetic field may fall off rapidly.

**[0104]** With the foregoing issues in mind, one embodiment of the present disclosure is directed to a microcoil array fabricated on a semiconductor (e.g., Si) substrate using conventional CMOS process technology. In one aspect of this embodiment, various field control components, including control electronics for the microcoil array, are integrated together with the microcoil array and fabricated as a CMOS IC chip, so as to provide for the generation of spatially and/or temporally variable magnetic fields for sample manipulation, as well as RF fields to facilitate sample detection, imaging and characterization. In particular, in exemplary implementations, the microcoils themselves are formed using standard CMOS protocols and hence do not require any micromachining techniques (e.g., as in microelectro-mechanical structures, or MEMS implementations).

**[0105]** More specifically, to address the design issues noted above, according to one embodiment multiple metal layers available in a CMOS fabrication process are employed in the microcoil configuration to allow generation of adequate magnetic field strengths sufficient to effectively trap and transport samples. **FIGS. 7(a)** and **7(b)** show perspective and exploded views, respectively, of an exemplary three-layer microcoil **212** according to this embodiment, and **FIG. 8** conceptually illustrates a vertical layer structure of a portion of a CMOS IC chip **102** showing the three-layer microcoil in relation to other features and layers of the overall chip structure. A  $z$  axis corresponding to that shown in **FIGS. 2 and 6(a)** is also indicated in **FIGS. 7 and 8**. It should be appreciated that the exemplary three-layer microcoil structure shown in **FIGS. 7 and 8** is provided primarily for purposes of illustration, and that microcoils according to other embodiments may include different numbers of layers (e.g., two or more) and/or have different overall shapes or geometries. In general, according to various embodiments, microcoils similar to those shown in **FIGS. 7 and 8** may include at least two axially concentric spatially separated portions (e.g., layers) of conductor turns.

**[0106]** As illustrated in **FIGS. 7 and 8**, the exemplary microcoil **212** includes three coiled conductor portions or layers, namely, an upper portion **212A**, a middle portion **212B** and a lower portion **212C**. To facilitate precision spatial control of individual magnetic samples contained in the microfluidic system above an array of microcoils **212**, each microcoil is designed to generate a single magnetic field peak above the microcoil to interact with samples. For example, as illustrated conceptually in **FIG. 8**, a magnetic sample **116** (e.g., a bead-bound cell, as also shown in **FIG. 6(b)**) suspended in a liquid contained in the microfluidic system **300** is attracted to a magnetic field peak generated above the microcoil **212** when an appropriate current flows through the microcoil. In **FIG. 8**, a distance between the upper portion **212A** of the microcoil (as fabricated in the overall layered structure of the IC chip **102**), and a bottom or floor of the microfluidic system **300** is indicated with the reference numeral **120**.

**[0107]** As discussed generally above, the principle of operation of the microcoil array **200B** for magnetic sample manipulation is to create and move one or more magnetic field peaks by modulating currents in the respective microcoils **212** of the array. For example, consider first “turning on” (i.e., passing current through) only one microcoil **212** of the array (e.g., the microcoil shown in **FIG. 8**); as shown in **FIG. 8**, the magnetic sample **116** is attracted to a magnetic field peak generated by the microcoil **212** and is thus trapped at the center of the microcoil above the surface of the IC chip **102**. Near the generated magnetic field peak, the “trapping force” is given by

$$F = V \chi / \mu_0 \nabla B^2, \quad (1)$$

where  $V$  is the volume of the magnetic bead **112**,  $\chi$  is the effective magnetic susceptibility of the bead,  $\mu_0$  is the magnetic permeability of a vacuum, and  $B$  is the generated magnetic field magnitude. If this microcoil is then “turned off” while an adjacent microcoil of the array is turned on, the magnetic field peak is moved to the center of the adjacent microcoil, thereby transporting the magnetic bead to the new peak location.

**[0108]** The magnetic field  $B$  required to generate a particular trapping force  $F$  is proportional to the current flowing